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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Denis P. Snider
Appl'n. No.	:	08/634,039
Filed	:	April 7, 1996
Title	:	METHODS AND COMPOSITIONS CONTAINING ANTIGENS HAVING A TARGETING MOIETY SPECIFIC FOR ANTIGEN PRESENTING CELS FOR INTRANASAL IMMUNIZATION
Grp./A.U.	:	1644
Examiner	:	F. VanderVegt
Docket No.	:	1038-588 MIS:as

February 21, 2001

RESPONSE TO OFFICE ACTION AND REQUEST FOR EXTENSION OF TIME

BY COURIER

The Commissioner of Patents
and Trademarks,
Washington, D.C. 20231,
U.S.A.

Sir:

This Communication is in response to the Office Action of August 22, 2000.

Petition is hereby made under the provisions of 37 CFR 1.136(a) for an extension of three months of the period for response to the outstanding Office Action on this case. We enclose our cheque in the amount of the prescribed fees.

The courtesy of the Examiner in granting an Interview on this application to the applicant's representative, Mr. Michael Stewart, and to Mr. Reza Yacoob, a member of the Patents Department of the Assignee, Connaught Laboratories Limited, is much appreciated. It is believed that the Interview was material in advancing the prosecution of this application. The Interview Summary

reflects the substance of the discussion with the Examiner at the Interview. The comments and submissions made herein complement and supplement those made to the Examiner at the Interview.

In the Office Action, the Examiner rejected claims 1 to 9 under 35 USC 103(a) as being unpatentable over Estrada et al in view of McDermott et al and Hameleers et al. Reconsideration is requested having regard to the following comments.

Applicants claims are directed to a method of generating an immune response to an antigen coupled to a targeting moiety specific for surface structures of antigen-presenting cells. Having regard to the prior art, it is submitted that it is surprising that a strong immune response to the antigen can be evoked by intranasal administration.

Estrada et al is concerned with experiments conducted to employ immunotargeting for oral immunization. The technique of immunotargeting is the method of conferring protection against pathogenic organisms by parenteral administration using monoclonal antibodies specific for membrane determinants expressed on mammalian antigen presenting cells as a targeting moiety, which are coupled to antigens derived from pathogenic organisms. This technique is described in the Barber patents of record herein and no longer relied on by the Examiner.

The results which are described (p. 904, right-hand column) in this reference indicate the weak and inconsistent production of intestinal IgA-antibody while serum IgG and IgA responses could be optimized by high doses of antigen. A significant mouse-to-mouse variation in antibody response was apparent within any immunization group, leading to a study of direct injection into the duodenum.

The article alluded to ongoing work but there is no subsequent paper by this group, involving the inventor herein, describing the results of such further studies and hence it must be concluded that mucosal administration effects orally to Peyer's patches was not sufficiently promising to merit further work and the approach simply was abandoned.

As previously submitted, it is considered unobvious that monoclonal antibodies or antibody-antigen conjugates applied to the epithelial surfaces of the nasal passages would be able to reach circulation or even the underlying lymphoid tissues of the epithelium in substantial quantity. A person skilled in the art would understand that the epithelial layers of the nasal passages have tight junctions and that large macromolecules, such as antibodies and conjugates, do not pass through the epithelium, except with very poor efficiency.

The antibodies used in applicant's experimentation have specificity for class II MHC molecules, expressed by APC. These class II MHC molecules are only poorly expressed by non-inflamed nasal epithelial cells of young rodents, as described in the Hameleers et al reference cited in response to the previous rejection, such as the mice that applicant immunized. In addition, there is no evidence that MHC class II molecules are expressed on the external membrane (apical surface) of rodent nasal epithelial cells. Available immunohistochemistry suggests only intracellular localization of class II MHC in the rodent nasal epithelium and those published results cannot define apical expression, as described in the Koornstra et al reference to which attention was drawn in response to the prior Office Action.

Having regard thereto and the work described in Estrada et al, the applicant had no reason to believe that the antibody conjugate would bind specifically to the epithelium or be taken up by the epithelium based on anti-class II MHC specificity.

It is submitted that the secondary references do not remedy the defects of Estrada et al. McDermott et al is a discussion of immunity in the respiratory tract, which possesses lymphoid aggregates similar to the Peyer's patches of the intestinal tract. As the Examiner observes:

> "McDermott et al ... teaches that the gut can be viewed as a model for the lung and that studies of oral immunization can provide insight into respiratory tract immunization" .

With respect to Hameleers et al, this reference teaches that nasal administration by KLH induced the production of IgA and IgG antibodies to TNP by administration of

the immungen as liquid drops.

It is submitted that there is no motivation provided by the results reported by Estrada et al for any expectation of success in achieving an immune response utilizing immunotargeting by intranasal administration of an antigen coupled to a targeting moiety specific for surface structures of antigen-presenting cells.

Accordingly, it is submitted that claims 1 to 9 are patentable over the applied art and hence the rejection thereof under 35 USC 103(a) as being unpatentable over Estrada in view of McDermott et al and Hameleers et al, should be withdrawn.

The Examiner rejected claims 1 to 9 under 35 USC 103(a) as being unpatentable over Estrada et al in view of McDermott et al, Hameleers et al and Babington.

The references, with the exception of Babington have been fully discussed above. The Babington reference is relied on for the teaching of a nebulizer which can be used to aerosolize medicaments for nasal inhalation. This teaching would not appear to remedy the defects of the basic combination of prior art, as discussed above.

Accordingly, it is submitted that claims 1 to 9 are patentable over the applied combination of prior art and hence the rejection of claims 1 to 9 under 35 USC 103(a) as being unpatentable over Estrada et al in view of McDermott et al, Hameleers et al, should be withdrawn.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,

SIM & McBURNEY

BY: M.I. Stewart

M.I. Stewart
Reg. No. 24,973

Toronto, Ontario, Canada,
(416) 595-1155
FAX No. (416) 595-1163

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ENCLOSURES *(check all that apply)*

- [ ] Fee Transmittal Form
- [X] Fee Attached
- [X] Amendment / Response
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [X] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Michael I. Stewart - Reg. No. 24,973
Signature	M. I Stewart
Date	February 21, 2001

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